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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,748	01/29/2001	Hisashi Narimatsu	1241.17	4282

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/03/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,748	NARIMATSU ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *19-23,25-50 and 54-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,24 and 51-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-75 are currently pending in this application. Claims 1-18, 24, 51-53 are now under consideration. Claims 19-23, 25-50, 54-75 are withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

Applicant's election of Group I, claims 1-18, 24, 51-53 in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 7 and 52 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 7 and 52 are directed to transformants having the

recombinant DNA according to claim 5 and 8 respectively. However, as claims dependent on claim 7 or 52 are further drawn to non-human transgenic animals, claims 7 and 52 would broadly include humans as transformants (even though applicants may not intend to claim as such) and would read on non-statutory subject matter. In view of this Examiner suggests that claims 7 and 52 be amended to be directed to "non-human transformants" or a "transformed cell" with appropriate amendments to specific dependent claims which claim transgenic animals as "non-human transgenic animals comprising the transformed cell of claim 7 or 52".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 recites the phrase "under stringent conditions". It is not clear to the Examiner as to what applicants mean by the above phrase. A perusal of the specification does not indicate a specific definition for the above phrase or specific conditions in terms of salt concentrations and time and temperature for hybridization and washing thus rendering the claims indefinite.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 12 recites the phrase "and collecting said polypeptide from said medium".

It is not clear to the Examiner as to what applicants mean by the above phrase as the polypeptide expressed by the cultured transformants would have already collected in the medium. Examiner suggests amending the claim to read as "isolating said polypeptide from the medium" in order to overcome this rejection.

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 13 recites the phrase "and collecting said polypeptide". It is not clear to the Examiner as to what applicants mean by the above phrase as the polypeptide expressed by the transgenic animal would have already collected in the animal. Examiner suggests amending the claim to read as "isolating said polypeptide from the animal" in order to overcome this rejection.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 15 recites the phrase "and collecting said polypeptide from said transgenic plant". It is not clear to the Examiner as to what applicants mean by the above phrase as the polypeptide expressed by the cultured transformants would have already collected in the plant. Examiner suggests amending the claim to read as "isolating said polypeptide from the plant" in order to overcome this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim6 is rejected because the invention appears to employ novel vectors. Since the vectors are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmids' sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the plasmids. The specification does not disclose a repeatable process to obtain the vectors and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of these plasmids should have been made in accordance with 37 CFR 1.801-1.809.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

Claims 1-18, 24, 51-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an enzyme with SEQ ID NO:1 or 2 having the activity of transferring fucose to an N-acetylglucosamine structure in an N-acetyllactosamine structure existing in a nonreducing terminus of a sugar chain via an alpha 1,3-linkage, but not having a similar activity to transfer fucose to N-acetylglucosamine residue in an alpha 2,3-sialyl N-acetyllactosamine structure, encoded by the polynucleotide with SEQ ID NO:3, 4, or 5, does not reasonably provide enablement for all such enzymes isolated from any source or such enzymes in which one or more amino acids are deleted substituted or added comprising variants, mutants and recombinants or any such enzyme encoded by a polynucleotide that can hybridize to SEQ ID NO:3, 4, or 5 or portions thereof under any type of stringent conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-18, 24, 51-53 are so broad as to encompass any alpha 1,3-fucosyltransferase isolated from any source including variants, mutants and recombinants that selectively fucosylates N-acetylglucosamine via alpha 1,3-linkage. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large

number of such enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single human alpha 1,3-fucosyltransferase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any alpha 1,3-fucosyltransfaase that exhibits the selective property described above because the specification does not establish: (A) regions of the protein structure which may be modified without effecting such activity; (B) the general tolerance of such alpha 1,3-fucosyltransferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any alpha 1,3-fucosyltransferase residues with an expectation of obtaining the desired biological function; and (D) the specification provides

insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any or all such alpha 1,3,-fucosyltransferase or such enzymes with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of alpha 1,3-fucosyltransferases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-18, 24, 51-53 are directed to polypeptides having the activity of transferring fucose to an N-acetylglucosamine structure in an N-acetyllactosamine structure existing in a nonreducing terminus of a sugar chain via an alpha 1,3-linkage, but not having a similar activity to transfer fucose to N-acetylglucosamine residue in an alpha 2,3-sialyl N-acetyllactosamine structure. Claims 1-18, 24, 51-53 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO:1 or 2 including

modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid and fragments that have not been disclosed in the specification. No description has been provided of all the polypeptide sequences encompassed by the claims. No information, beyond the characterization of SEQ ID NO:1 and 2 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the structure of all the polypeptide sequences derived from SEQ ID NO:1 or 2, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a two species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 8, 9, 12, 17, 18, 24, 51, 52, 53 are rejected under 35 U.S.C. 102(a) as being anticipated by Ge et al. (J. Biol. Chem. Vol., 272(34):21357-21363, Aug. 1997). This rejection is based upon the public availability of a printed publication. Claims 1-7, 8, 12, 17, 18, 24, 51, 52, 53 of the instant application is drawn to an enzyme having the activity of transferring fucose to an N-acetylglucosamine structure in an N-acetyllactosamine structure existing in a nonreducing terminus of a sugar chain via an alpha 1,3-linkage, but not having a similar activity to transfer fucose to N-acetylglucosamine residue in an alpha 2,3-sialyl N-acetyllactosamine structure and variants or mutants of such an enzyme in which one or more amino acids are deleted substituted or and enzymes which are encoded by a polynucleotide which hybridizes under(undefined) stringent conditions to SEQ ID NO:2, 3 or 5, polynucleotides encoding such enzymes, vectors and host cells (transformants) including E.coli cells comprising such polynucleotides and methods of making such polypeptide by culturing said host cells. Claims are also drawn to method of making reaction products using such enzymes. Ge et al. disclose an enzyme with identical properties (see abstract and the entire publication), polynucleotide which encodes such enzymes, vectors and transformants comprising such polynucleotides and method of making such polypeptides and use it in a reaction to make reaction products. Since there is no limitation placed on the number of changes that can be present in the polypeptide or polynucleotide sequence for a variant polypeptide or the hybridizing polynucleotide, above claims read on the enzyme and the DNA sequence disclosed by Ge et al. Thus Ge et al. anticipate claims 1-7, 8, 12, 17, 18, 24, 51, 52, 53 of this application as written.

Claims 1-7, 8, 12, 17, 18, 24, 51, 52, 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Lowe et al. (J. Biol. Chem. Vol., 266(26):17467-17477, Sep. 1991). This rejection is based upon the public availability of a printed publication. Claims 1-7, 8, 12, 17, 18, 24, 51, 52, 53 of the instant application is drawn to an enzyme having the activity of transferring fucose to an N-acetylglucosamine structure in an N-acetyllactosamine structure existing in a non reducing terminus of a sugar chain via an alpha 1,3-linkage, but not having a similar activity to transfer fucose to N-acetylglucosamine residue in an alpha 2,3-sialyl N-acetyllactosamine structure and variants or mutants of such an enzyme in which one or more amino acids are deleted substituted or and enzymes which are encoded by a polynucleotide which hybridizes under(undefined) stringent conditions to SEQ ID NO:2, 3 or 5, polynucleotides encoding such enzymes, vectors and host cells (transformants) including mammalian cells comprising such polynucleotides and methods of making such polypeptide by culturing said host cells. Claims are also drawn to method of making reaction products using such enzymes. Lowe et al. disclose an enzyme with identical properties (see abstract and the entire publication), polynucleotide which encodes such enzymes, vectors and transformants comprising such polynucleotides including a mammalian cell such as COS-1 and method of making such polypeptides and use said polypeptide in a reaction to make reaction products. Since there is no limitation placed on the number of changes that can be present in the polypeptide or polynucleotide sequence for a variant polypeptide or the hybridizing polynucleotide, above claims read on the enzyme and the DNA sequence disclosed by Lowe et al. Thus Lowe et al. anticipate claims 1-7, 8, 12, 17, 18, 24, 51, 52, 53 of this application as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-11, 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Ge et al. or Lowe et al. as applied to claims 1-9, 12, 17, 18, 24, 51, 52, 53 above, and further in view of the high level of knowledge in the art of molecular biology. Claims 10-11, 13-16 in this instant application are drawn to transformants wherein the transformants are specific animal cells or insect cells and to method for producing the polypeptide by using the milk of a transgenic animal or the plant parts of a transgenic plant or an in vitro method of translation wherein the DNA encoding the polypeptide is translated using an in vitro translation system. The references of Ge et al. and Lowe et al. have already been discussed above. While both the above references teach the polypeptide, polynucleotide, vector and a transformant and a method of making the polypeptide by culturing the transformant, the above references however do not teach the specific host cells for transformation or the transgenic plant or the animal and method of producing the polypeptide using the part of the plant or the milk of the animal or the in vitro method of translation as claimed in the above claims.

With the above two references in hand, it would have been obvious to one of ordinary skill in the art to choose any of the above cells for transformation or produce the polypeptide by use of transgenic plants or animals since such techniques are well known in the art and are routinely used for bulk preparation of the heterologous polypeptides. One of ordinary skill in

the art would have been motivated to do so because the polypeptide having the above activity has been recognized in the art as useful in preparation of specific carbohydrate structures which has applications in diagnosis of certain human disorders. One of ordinary skill in the art would have a reasonable expectation of success because the above references provide the purified polynucleotide expressing the above polypeptide and the art is rich in several of the techniques to perform the above experiments and also provides step by step guidance.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 6:30 a.m. to 3:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is

(703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Manjunath N. Rao Ph.D.
11/21/02